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EXAMINER	
RAMIREZ, DELIA M	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/777,566	SHORT ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13,16-33,35,36,38-43,45,46 and 81-98* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,16-33,35,36,38-43,45,46 and 81-98* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *alignment*.

DETAILED ACTION

Status of the Application

Claims 1-13, 16-33, 35-36, 38-43, 45-46, 81-98 are pending.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/27/2006 has been entered.

Applicant's amendment of claims 1-2, 8, 10, 11-13, 16, 35-36, 38-43, 45-46, cancellation of claims 34, 37, 47-80, and addition of claims 81-98 as submitted in a communication filed on 4/27/2006 is acknowledged. Claims 1-13, 16-33, 35-36, 38-43, 45-46, 81-98 are at issue and are being examined herein.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Information Disclosure Statement

1. Applicant requests that the Examiner consider the IDS filed on 1/6/2006 and an IDS filed with the response of 4/27/2006. It is noted, however, that the Examiner did consider the IDS filed on 1/6/2006 and indicated such action in the Advisory action mailed on 4/10/2006 (see item 3 of the Advisory action and PTO-303, item 13). With regard to a new IDS filed concurrently with the response of 4/27/2006, it is noted that there is no IDS filed after 1/6/2006 according to PTO records.

Specification

2. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See page 80, line 12 (NCBI entry). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

3. The specification is objected to due to the recitation on page 52, line 6 of "expression fo". It should be replaced with "expression of". Appropriate correction is required.

Claim Objections

4. Claims 2, 10, 11, 12, 16, 36, 38-43, 46, 92-94, 97-98 are objected to due to the recitation of "nucleotide sequence ...further comprising a homologous signal sequence or comprising a heterologous signal sequence in place of the homologous signal sequence", "nucleic acid of .... comprising a homologous signal sequence or comprising a heterologous signal sequence in place of the homologous signal sequence" for the following reasons. As known in the art, the term "signal sequence" generally refers to the sequence of a signal peptide. Thus, a nucleotide sequence would not comprise a peptide sequence. For examination purposes, it will be assumed that the terms read "comprising a sequence encoding a homologous signal sequence or comprising a sequence encoding a heterologous signal sequence...". Appropriate correction is required.

5. Claim 35 is objected to due to the recitation of "any of steps (i) to (v)" because (i)-(v) are not steps but rather nucleic acids. Appropriate correction is required.

6. Claims 83, 85-87 are objected to due to the recitation of "nucleic acid (1)(i) encoding a phytase comprising.....; (ii) comprising an amino acid sequence.....; (iii) comprising an amino acid sequence.." for the following reasons. As written, the claims are stating that the nucleic acid comprises an amino acid sequence. It is suggested the term be amended to recite "nucleic acid (1) encoding a phytase (i)

comprising.....; (ii) comprising an amino acid sequence.....; (iii) comprising an amino acid sequence..".

Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-13, 16-33, 35-36, 38-43, 45-46, 81-98 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claims 1-2, 10-12, 16, 35-36, 38-43, 45-46, 81-89, 92-94, 97-98 (claims 3-9, 13, 17-33, 90-91, 95-96 dependent thereon) are indefinite in the recitation of "comprising a homologous signal sequence or comprising a heterologous signal sequence in place of the homologous signal sequence" for the following reasons. Based on the teachings of the specification and those of the art, the phytase of SEQ ID NO: 2 (encoded by the polynucleotide of SEQ ID NO: 1) and amino acids 1-432 of the phytase of SEQ ID NO: 2 (encoded by nucleotides 1-1296 of the polynucleotide of SEQ ID NO: 1) already contain an endogenous signal sequence which is at the N-terminus. Thus, it is unclear as to how the terms further limit the claims (i.e., there is redundancy since the polypeptide of SEQ ID NO: 2 (or amino acids 1-432 thereof) already contains a "homologous" signal sequence), or whether the terms imply that the phytase of SEQ ID NO: 2 (or amino acids 1-432 thereof) does not include a "homologous" signal sequence (i.e., the polypeptide of SEQ ID NO: 2 (or amino acids 1-432 thereof) is a mature protein lacking its endogenous signal peptide). For examination purposes, the Examiner will interpret the terms as reading "comprising a heterologous signal sequence in place of the endogenous signal sequence". Correction is required.

10. Claims 46, 81 are indefinite in the recitation of "wherein the exogenous nucleic acid (i)...., (iv) comprising a nucleotide sequence as set forth in (i), (ii), or (iii) but lacking a signal sequence" as it is

unclear how the nucleotide sequence set forth in (iii) lacking a signal sequence is any different from the nucleotide sequence set forth in (i)-(ii) lacking a signal sequence. For examination purposes, no patentable weigh has been given to the term "or (iii)". Correction is required.

11. Claims 92-94, 97-98 (claims 95-96 dependent thereon) are indefinite in the recitation of "lacking a leader sequence" for the following reasons. As indicated above, the polypeptide of SEQ ID NO: 2 contains an endogenous signal peptide for secretion into the periplasmic space at the N-terminus. Thus, it is unclear as to whether the term "leader sequence" refers to the sequence of the signal peptide or if it refers to something else. In addition, if the term "leader sequence" is meant to be equivalent to "signal sequence", it is unclear as to how the polypeptide/polynucleotide set forth in (iii) or (vi) lacking a "leader sequence" is any different from the polypeptide/polynucleotide set forth in (i), (ii), (iv), (v) lacking a "leader sequence". For examination purposes, no patentable weight will be given to items (viii)-(ix). Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 1-13, 16-33, 35, 46, 81, 82, 92-95, 97-98 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 1-13, 16-33, 35, 46, 81, 82, 92-95, 97-98 require nucleic acids encoding a protein comprising SEQ ID NO: 2 (or amino acids 1-432 of SEQ ID NO: 2) further comprising a sequence

imparting a desired characteristic. While the specification provides support for nucleic acids encoding fusion proteins and provides support for a nucleic acid encoding a fusion enzyme including an N-terminal identification peptide imparting desired characteristics (page 40, last sentence), the Examiner is unable to find support for a nucleic acid encoding a protein further comprising any sequence imparting a desired characteristic. Thus there is no indication that the instant genus of nucleic acids were within the scope of the invention as conceived by Applicants at the time the application was filed. Accordingly, Applicants are required to cancel the new matter in the response to this Office Action.

14. Claims 10-13, 24-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 10-11, 24-27 require a polypeptide comprising "an amino acid sequence" of SEQ ID NO: 2 or amino acids 1-432 of SEQ ID NO: 2, due to the recitation in claims 10-11 of "(vi) comprises an amino acid sequence of (iv) or (v)". Claims 12-13, 28-33 require a polypeptide comprising "an amino acid" of the polypeptide of SEQ ID NO: 2 or a polypeptide comprising amino acids 1-432 of SEQ ID NO: 2, due to the recitation in claim 12 of "(vi) comprises an amino acid of (iv)...".

As stated in MPEP 2111.01, during examination, the claims must be interpreted as broadly as their terms reasonably allow. While the term "the amino acid sequence of X" clearly indicates that the amino acid sequence contains all of X, the term "an amino acid sequence of X", as recited in claims 10-11 can be interpreted as "an amino acid sequence within X" (i.e., not all of X). Thus, in the instant case, the Examiner has broadly interpreted the term "an amino acid sequence of X" to encompass a fragment of at least 2 amino acids of SEQ ID NO: 2 or amino acids 1-432 of SEQ ID NO: 2. Similarly, the Examiner has broadly interpreted the term "an amino acid of X" to encompass any amino acid within

SEQ ID NO: 2 or within amino acids 1-432 of SEQ ID NO: 2. In view of this interpretation, claims 10-11, 24-27 are directed in part to a prokaryotic or eukaryotic cell comprising an exogenous nucleic acid encoding a phytase, wherein said phytase comprises any fragment of at least 2 amino acids of (1) the polypeptide of SEQ ID NO: 2, or (2) the segment of the polypeptide of SEQ ID NO: 2 containing amino acids 1-432 of SEQ ID NO: 2. Claim 12 is directed in part to a cell comprising an exogenous nucleic acid encoding a phytase, wherein said phytase comprises any amino acid within SEQ ID NO: 2 or within amino acids 1-432 of SEQ ID NO: 2. Claims 13, 28-33 are directed in part to a method for making a phytase which comprises any amino acid within SEQ ID NO: 2 or within amino acids 1-432 of SEQ ID NO: 2.

In *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". As indicated in MPEP § 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

In the instant case, the claims encompass a structurally diverse genus of polypeptides. While the specification discloses that the polypeptide of SEQ ID NO: 2 is a phytase, the specification fails to

disclose (1) other phytases comprising fragments of the phytase of SEQ ID NO: 2, (2) the specific amino acid fragments within SEQ ID NO: 2 which are essential for any polypeptide comprising them to display phytase activity, or (3) a correlation between structure and phytase activity.

While a sufficient written description of a genus of polypeptides may be achieved by a recitation of a representative number of polypeptides defined by amino acid sequence or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus, in the instant case, the structural features as interpreted, i.e., "any fragment of at least 2 amino acids of the polypeptide of SEQ ID NO: 2", "any fragment of at least 2 amino acids of the segment of the polypeptide of SEQ ID NO: 2 having amino acids 1-432 of SEQ ID NO: 2", or "any amino acid within SEQ ID NO: 2", do not constitute a substantial portion of the genus as the remainder of any polypeptide comprising said structural elements is completely undefined and the specification does not define the remaining structural features for members of the genus to be selected.

The genus of polypeptides recited is extremely variable in structure. While one could argue that the disclosure of the polypeptide of SEQ ID NO: 2 provides adequate description for all the members of the genus, it is noted that the art teaches several examples of how even small variations in structure can lead to functional variation. For example, Witkowski et al. (Biochemistry 38:11643-11650, 1999; cited in the IDS) teaches that mutations which result in one conservative amino acid substitution transform a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminate β-ketoacyl synthase activity. Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001) teaches that two naturally occurring Pseudomonas enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. Therefore, since (a) minor structural variations may result in changes affecting function, (b) there is no additional information correlating structure with phytase activity, (c) there is no teaching or suggestion as to which portions of the polypeptide of SEQ ID NO: 2 are required in any polypeptide such that it would have the same enzymatic activity as that of the

polypeptide of SEQ ID NO: 2, and (d) no information has been provided in regard to which amino acids in the polypeptide of SEQ ID NO: 2 can be modified and which ones need to be conserved to avoid loss of activity, one cannot reasonably conclude that the polypeptide of SEQ ID NO: 2 is representative of all the polypeptides as recited.

Due to the fact that the specification only discloses a single species of the claimed genus of polypeptides (i.e., SEQ ID NO:2), and the lack of description of any additional species by any relevant, identifying characteristics or properties, one of skill in the art would not recognize from the disclosure that Applicant was in possession of the claimed invention.

15. Claims 1, 3, 4, 6, 8, 10-13, 16-17, 19-23, 24-33, 36, 82-84, 86-88, 97 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated host cell comprising a nucleic acid encoding the polypeptide of SEQ ID NO: 2 or encoding amino acids 1-432 of SEQ ID NO: 2, as well as a method for recombinantly produce the polypeptide of SEQ ID NO: 2, or a polypeptide comprising amino acids 1-432 of SEQ ID NO: 2, does not reasonably provide enablement for (1) a non-isolated host cell comprising a nucleic acid encoding the polypeptide of SEQ ID NO: 2, or encoding amino acids 1-432 of SEQ ID NO: 2, (2) an isolated/non-isolated host cell comprising a nucleic acid encoding a phytase which comprises any fragment or any amino acid within (i) SEQ ID NO: 2, or (ii) amino acids 1-432 of SEQ ID NO: 2, or (3) a method to recombinantly produce the phytase of (2). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2nd 1400 (Fed. Cir. 1988)) as follows: (1) quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence and absence of working examples, (4) the nature of the invention, (5) the state of prior art, (6) the relative

skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breath of the claims. The factors which have lead the Examiner to conclude that the specification fails to teach how to make and/or use the claimed invention without undue experimentation, are addressed in detail below.

The breath of the claims. Claims 1, 3, 4, 6, 8, 10-13, 16-17, 19-23, 28-33, 36, 82-84, 86-88, 97 are so broad as to encompass (1) a prokaryotic or isolated/non-isolated eukaryotic cell comprising an exogenous nucleic acid encoding a phytase, wherein said phytase comprises any fragment of at least 2 amino acids of (i) the polypeptide of SEQ ID NO: 2, or (ii) the segment of the polypeptide of SEQ ID NO: 2 containing amino acids 1-432 of SEQ ID NO: 2, (2) an isolated/non-isolated cell comprising an exogenous nucleic acid encoding a phytase, wherein said phytase comprises any amino acid within SEQ ID NO: 2 or within amino acids 1-432 of SEQ ID NO: 2, (3) a method for making a phytase which comprises any amino acid within SEQ ID NO: 2 or within amino acids 1-432 of SEQ ID NO: 2, and (4) a non-isolated host cell comprising a nucleic acid encoding the polypeptide of SEQ ID NO: 2, or encoding amino acids 1-432 of SEQ ID NO: 2. See Claim Rejections under 35 USC 112, second paragraph, and Claim Rejections under 35 USC 112, first paragraph (written description) for claim interpretation and discussion of scope.

The enablement provided is not commensurate in scope with the claims due to the extremely large number of polynucleotides of unknown structure encompassed by the claims as well as the lack of information regarding the structural elements in the polypeptide of SEQ ID NO: 2 which are required in any polypeptide such that they would display phytase activity. In the instant case, the specification enables a polynucleotide encoding the polypeptide of SEQ ID NO: 2, and the polynucleotide of SEQ ID NO: 1.

With regard to claims 1, 3, 4, 6, 8, 11-12, 16-17, 19-23, 36, 82-84, 86-88, 97, it is noted that the specification states that a preferred embodiment is the administration of the phytase to organisms by using transgenic methods (page 52, lines 4-9). Therefore, in its the broadest reasonable interpretation, claims

1, 3, 4, 6, 8, 11-12, 16-17, 19-23, 36, 82-84, 86-88, 97 are directed not only to isolated host cells but also to host cells within a transgenic multicellular organism (i.e., non-isolated). The enablement provided is not commensurate in scope with the claim due to the extremely large number of transgenic multicellular organisms comprising the cells encompassed by the claims which the specification fails to teach how to generate or how to use. In the instant case, the specification enables an isolated host cell comprising the polynucleotide of SEQ ID NO: 1 (encodes the polypeptide of SEQ ID NO: 2).

The amount of direction or guidance presented and the existence of working examples. The specification discloses the nucleotide sequence of the polynucleotide of SEQ ID NO: 1 as well as the polypeptide sequence of the phytase of SEQ ID NO: 2, as working examples. However, the specification fails to provide any clue as to (1) a correlation between structure and phytase activity, (2) other phytases comprising fragments of any size of the polypeptide of SEQ ID NO: 2, (3) or the structural elements in the polypeptide of SEQ ID NO: 2 essential for phytase activity.

With regard to claims 1, 3, 4, 6, 8, 11-12, 16-17, 19-23, 36, 82-84, 86-88, 97, while the specification discloses that the polynucleotides of the invention can be used to transform isolated host cells for recombinant production of the corresponding polypeptides, to create transgenic plants, and to deliver the phytase of the invention to organism by transgenic methods, there are no working examples or specific methods disclosed showing a transgenic multicellular organism capable of expressing the recited polynucleotides.

The state of prior art, the relative skill of those in the art, and the predictability or unpredictability of the art. The nucleotide sequence of the coding region of a polynucleotide determines the structural and functional properties of the protein encoded by the polynucleotide. In the instant case, neither the specification nor the art provide a correlation between structure and activity such that one of skill in the art can envision the remaining structure of any phytase-encoding polynucleotide wherein the phytase comprises any fragment/any amino acid of the polypeptide of SEQ ID NO: 2. In addition, the art

does not provide any teaching or guidance as to (1) which amino acids within SEQ ID NO: 2 are required for phytase activity, (2) which amino acids within SEQ ID NO: 2 can be modified and which ones can be conserved such that variants of the polypeptide of SEQ ID NO: 2 would display the same phytase activity of the polypeptide of SEQ ID NO: 2, or (3) the general tolerance of phytases to structural modifications and the extent of such tolerance.

The art clearly teaches that changes in a protein's amino acid sequence to obtain the desired activity without any guidance/knowledge as to which amino acids in a protein are required for that activity is highly unpredictable. At the time of the invention there was a high level of unpredictability associated with altering a polypeptide sequence with an expectation that the polypeptide will maintain the desired activity. For example, Branden et al. (Introduction to Protein Structure, Garland Publishing Inc., New York, page 247, 1991) teach that (1) protein engineers are frequently surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes, (2) the often surprising results obtained by experiments where single mutations are made reveal how little is known about the rules of protein stability, and (3) the difficulties in designing *de novo* stable proteins with specific functions. The teachings of Branden et al. are further supported by the teachings of Witkowski et al. and Seffernick et al. already discussed above, where it is shown that even small amino acid variations result in enzymatic activity changes.

With regard to transgenic multicellular organisms, the prior art teaches that making genetically modified animals is highly unpredictable. The relevant art has for many years indicated that the unpredictability of generating transgenic animals lies with the site or sites of integration of the transgene into the target genome. Kappel et al. (Current Opinion in Biotechnology 3:548-553, 1992) teach that transgenic animals are known to have inherent cellular mechanisms which may alter the pattern of gene expression, such as DNA methylation or deletion from the genome (page 549, right column, third paragraph). Furthermore, Mullins et al. (Hypertension 22(4):630-633, 1993) teach that integration of a

transgene in different species may result in widely different phenotypic responses (page 631, left column, first paragraph, last sentence). Also, Mullins et al. (J. Clin. Invest. 97(7):1557-1560, 1996) teach that "the use of nonmurine species for transgenesis will continue to reflect the suitability of a particular species for the specific questions being addressed, bearing in mind that a given construct may react very differently from one species to another." (page 1559, Summary). Wigley et al. (Reprod. Fert. Dev. 6:585-588, 1994) indicate that transgenesis by microinjection has a number of limitations including random integration in the genome and integration of transgenes in multiple copies at one site such that expression level is not proportional to transgene copy number (page 585, Introduction). Cameron (Molecular Biotechnology 7:253-265, 1997) teaches that well-regulated expression of the transgene is not frequently achieved because of poor levels or the complete absence of expression or leaky expression in non-target tissues (page 256, left column, last three lines, right column, first three lines). According to Cameron, transgene expression with different transgenic lines produced with the same constructs is unpredictable and expression levels do not correlate with the number of transgene copies integrated, thus indicating the influence of the integration site on the expression pattern (page 256, right column, lines 3-13).

The quantity of experimentation required to practice the claimed invention based on the teachings of the specification. While methods of generating or isolating variants of a polynucleotide were known in the art at the time of the invention, it was not routine in the art to screen by a trial and error process for all the polynucleotides encoding polypeptides having phytase activity. In the absence of (1) a rational and predictable scheme for modifying any amino acid in the polypeptide of SEQ ID NO: 2 such that the resulting variant would have the same enzymatic activity as that of the polypeptide of SEQ ID NO: 2, and/or (2) a correlation between structure and phytase activity, one of skill in the art would have to assay an extremely large number of polynucleotides to find those which encode polypeptides having phytase activity.

While current screening techniques in the art would allow for testing a limited number of species, testing the essentially infinite number of polynucleotides recited in the claims would not be possible. Therefore, while enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, as is the case herein, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed so that a reasonable number of species can be selected for testing. In view of the fact that such guidance has not been provided in the instant specification, it would require undue experimentation to enable the full scope of the claims. Furthermore, given the teachings of the art regarding the differences in expression of a transgene in different species, the limitations regarding the integration and expression of a transgene, and in view of the lack of guidance provided by the specification, it would require undue experimentation to engineer any transgenic multicellular organism comprising the cells claimed.

Therefore, taking into consideration the extremely broad scope of the claims, the lack of guidance, the amount of information provided, the lack of knowledge about a correlation between structure and function, the high degree of unpredictability of the prior art in regard to (a) structural changes and their effect on function, and (b) generation of transgenic multicellular organisms, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to practice the claimed invention. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

17. Claims 10-13, 24-33 are rejected under 35 U.S.C. 102(a) and 102(e) as being anticipated by Van Ooijen et al. (U.S. Patent No. 5593963, issued on 1/14/1997, filed on 11/2/1993; cited in the IDS).

Claims 10-11, 24-27 are directed in part to a prokaryotic or plant cell/seed cell comprising an exogenous nucleic acid encoding a phytase, wherein said phytase comprises any fragment of at least 2 amino acids of (1) the polypeptide of SEQ ID NO: 2, or (2) the segment of the polypeptide of SEQ ID NO: 2 containing amino acids 1-432 of SEQ ID NO: 2, wherein the plant cell is a cell from any number of fruits and vegetables, including an apple cell, potato cell, and rapeseed cells. Claim 12 is directed in part to a cell comprising an exogenous nucleic acid encoding a phytase, wherein said phytase comprises any amino acid within SEQ ID NO: 2 or within amino acids 1-432 of SEQ ID NO: 2. Claims 13, 28-33 are directed in part to a method for making a phytase which comprises any amino acid within SEQ ID NO: 2, or within amino acids 1-432 of SEQ ID NO: 2, wherein said method requires culturing a prokaryotic or plant cell/seed cell which expresses a nucleic acid encoding the phytase, wherein said method further comprises converting the cell into a composition suitable for animal feed, and wherein the plant cell is a cell from any number of fruits and vegetables, including an apple cell, potato cell, and rapeseed cells. See Claim Rejections under 35 USC 112, first paragraph for discussion of claim interpretation and scope.

Van Ooijen et al. teach a phytase which comprises several fragments of at least two amino acids of SEQ ID NO: 2. See attached alignment. For example, the phytase of Van Ooijen et al. comprises amino acids 37-40 of SEQ ID NO: 2 of the instant application (amino acids 80-83 of SEQ ID NO: 20 of U.S. Patent No. 5593963; amino acids 57-60 of SEQ ID NO: 20 if amino acid # 1 is the first amino acid

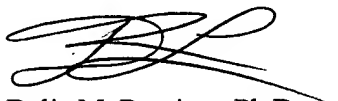
of the mature protein). Van Ooijen et al. teach the polynucleotide encoding the phytase (SEQ ID NO: 19), bacterial host cells producing the phytase wherein said cells are transformed with an expression vector comprising said polynucleotide (Example 4, column 12, lines 26-30; *A. tumefaciens* strain LBA4404), tobacco seed cells expressing the polynucleotide encoding the phytase (Example 8, column 15); transformation of rapeseed cells with the polynucleotide encoding the phytase (Example 9, column 16), production of the phytase in transformed cells from any number of fruits and vegetables, including apple cells, potato cells and rapeseed cells (column 5, line 66-column 6, line 26), and converting the transformed cells producing the phytase into a composition suitable for animal feed (column 9, lines 36-41). Therefore, the teachings of Van Ooijen et al. anticipate the instant claims as written.

Conclusion

18. No claim is in condition for allowance.

19. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.



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DR
June 24, 2006